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NEWS	1		Web Page for STN Seminar Schedule - N. America
NEWS	2	AUG 10	Time limit for inactive STN sessions doubles to 40 minutes
NEWS	3	AUG 18	COMPENDEX indexing changed for the Corporate Source (CS) field
NEWS	4	AUG 24	ENCOMPLIT/ENCOMPLIT2 reloaded and enhanced
NEWS	5	AUG 24	CA/CAplus enhanced with legal status information for U.S. patents
NEWS	6	SEP 09	50 Millionth Unique Chemical Substance Recorded in CAS REGISTRY
NEWS	7	SEP 11	WPIDS, WPINDEX, and WPIX now include Japanese FTERM thesaurus

NEWS EXPRESS MAY 26 09 CURRENT WINDOWS VERSION IS V8.4,
AND CURRENT DISCOVER FILE IS DATED 06 APRIL 2009.

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FILE 'HOME' ENTERED AT 17:34:06 ON 19 OCT 2009

=> file hcaplus

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.22	0.22

FILE 'HCAPLUS' ENTERED AT 17:34:33 ON 19 OCT 2009
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Updated Search

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FILE COVERS 1907 - 19 Oct 2009 VOL 151 ISS 17
FILE LAST UPDATED: 18 Oct 2009 (20091018/ED)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Aug 2009
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Aug 2009

HCAplus now includes complete International Patent Classification (IPC)
reclassification data for the third quarter of 2009.

CAS Information Use Policies apply and are available at:

http://www.cas.org/legal/infopolicy.html

This file contains CAS Registry Numbers for easy and accurate
substance identification.

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=> s neoplastic () disease
         71586 NEOPLASTIC
            24 NEOPLASTICS
         71604 NEOPLASTIC
                  (NEOPLASTIC OR NEOPLASTICS)
       1186801 DISEASE
        330238 DISEASES
       1333537 DISEASE
                  (DISEASE OR DISEASES)
L1        2745 NEOPLASTIC (W) DISEASE

=> s l1 () inhibit?
       2189130 INHIBIT?
L2           6 L1 (W) INHIBIT?

=> s l2 and review/dt
       2306050 REVIEW/DT
L3           0 L2 AND REVIEW/DT

=> d l2, ibib abs, 1-6
THE ESTIMATED COST FOR THIS REQUEST IS 18.00 U.S. DOLLARS
DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N:y

L2   ANSWER 1 OF 6  HCAPLUS  COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER:         2006:1066837  HCAPLUS
DOCUMENT NUMBER:          145:419133
TITLE:                    Preparation of 1-substituted pyrazolo[3,4-c]pyridines,
```

6,7,8,9-tetrahydro/pyrazolo[3,4-c]quinolines, and pyrazolo[3,4-c]naphthyridines as modulators of cytokine biosynthesis for treatment of viral and neoplastic diseases

INVENTOR(S): Hays, David S.; Prince, Ryan B.; Haraldson, Chad A.; Bonk, Jason D.

PATENT ASSIGNEE(S): 3M Innovative Properties Company, USA

SOURCE: PCT Int. Appl., 152pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006107851	A1	20061012	WO 2006-US12263	20060331
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
AU 2006232375	A1	20061012	AU 2006-232375	20060331
CA 2602590	A1	20061012	CA 2006-2602590	20060331
EP 1863814	A1	20071212	EP 2006-749140	20060331
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, YU				
JP 2008538550	T	20081030	JP 2008-504494	20060331
US 20090163533	A1	20090625	US 2008-887492	20081114

PRIORITY APPLN. INFO.:

US 2005-667869P	P	20050401
US 2005-733037P	P	20051103
WO 2006-US12263	W	20060331

OTHER SOURCE(S): CASREACT 145:419133; MARPAT 145:419133

GI

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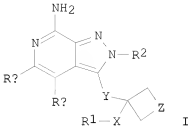

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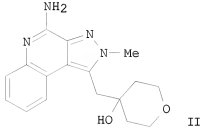

II

AB Title compds. [I; Z = a bond, alkylene, (CH2)0-2-O-(CH2)0-2; o-phenylene, etc.; X = a bond, alkylene, -O-alkylene-; R1 = H, OH and derivs., F, NH2 and derivs., etc.; Y = (CH2)m; m = 1-5; RA, RB = independently H, halo, alk(en)yl, alkoxy, alkylthio, NH2 and derivs.; or RACCRB = fused hetero/aryl, or fused 5-7 membered saturated ring; R2 = H, alkyl, alkoxyalkenyl, haloalkenyl, etc.; and their pharmaceutically acceptable salts; with provisos] were prepared as immunomodulators for inducing cytokine biosynthesis in animals and in the treatment of diseases including viral and neoplastic diseases. For example, bromination of 5-[(4-hydroxytetrahydro-2H-pyran-4-yl)methyl]-1-methyl-1H-pyrazole-3-carbonitrile(preparation given), coupling with 2-aminophenylboronic acid•HCl and cyclization gave pyrazoloquinoline II (no data for the coupling intermediate). Certain I modulated cytokine biosynthesis by inducing the production of interferon α and/or tumor necrosis factor α when tested in human cells (no data).

OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 2 OF 6 HCAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2005:493478 HCAPLUS

DOCUMENT NUMBER: 143:43875

TITLE: Preparation of hydroxylamine and oxime substituted imidazoquinolines, imidazopyridines, and imidazonaphthyridines as inducers of cytokine biosynthesis for treatment of viral and neoplastic diseases

INVENTOR(S): Krepski, Larry R.; Dellaria, Joseph F., Jr.; Duffy, Daniel E.; Amos, David T.; Zimmermann, Bernhard M.; Squire, David J.; Marszalek, Gregory J.; Heppner, Philip D.; Kshirsagar, Tushar A.

PATENT ASSIGNEE(S): 3M Innovative Properties Company, USA

Updated Search

STN

SOURCE: PCT Int. Appl., 305 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005051324	A2	20050609	WO 2004-US39673	20041124
WO 2005051324	A3	20060105		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004293096	A1	20050609	AU 2004-293096	20041124
CA 2547085	A1	20050609	CA 2004-2547085	20041124
EP 1686992	A2	20060809	EP 2004-812235	20041124
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, IS				
CN 1905874	A	20070131	CN 2004-80040953	20041124
JP 2007512349	T	20070517	JP 2006-541442	20041124
US 20070099901	A1	20070503	US 2006-595859	20060518
IN 2006CN01847	A	20070608	IN 2006-CN1847	20060525
ZA 2006005216	A	20070425	ZA 2006-5216	20060623

PRIORITY APPLN. INFO.:	US 2003-524961P	P	20031125
	US 2004-580139P	P	20040616
	US 2004-581293P	P	20040618
	WO 2004-US39673	W	20041124

OTHER SOURCE(S): CASREACT 143:43875; MARPAT 143:43875
GI

Updated Search

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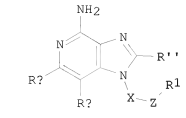

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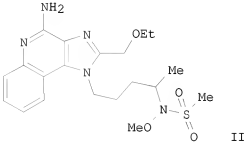


II

AB Title compds. [I; Z = -C(:N-OR2)- or CH-N(OR2)(YR3); X = CHR9,-CH(R9)-alk(en)ylene-, etc.; R9 = H, alkyl; R1 = H, (un)substituted alkyl, alkylene/hetero/aryl, etc.; R2, R3 = independently H, (un)substituted alk(en)yl, hetero/aryl, hetero/arylalkylenyl, etc.; Y = a bond, C:O, C:S, SO2, etc.; RA, RB = independently H, halo, alk(en)yl, etc.; RACCRB = (un)substituted fused hetero/aryl, fused 5-7-membered saturated ring], were prepared as immunomodulators for inducing cytokine biosynthesis in animals and in the treatment of diseases including viral and neoplastic diseases. For example, reacting 5-[4-Amino-2-(ethoxymethyl)-1H-imidazo[4,5-c]quinolin-1-yl]pentan-2-one with NH2OH•HCl in the presence of NaBH3CN/AcOH/EtOH, and substitution with mesyl anhydride gave imidazoquinoline II (m.p. = 146-148°). Certain I may modulate cytokine biosynthesis by inhibiting production of tumor necrosis factor TNF-α when tested in mouse cells (no data).

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 3 OF 6 HCAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2005:490270 HCAPLUS

DOCUMENT NUMBER: 143:26611

TITLE: Preparation of oxime substituted imidazo-containing compounds, particularly imidazoquinolines, as inducers of cytokine biosynthesis for treatment of viral and neoplastic diseases

INVENTOR(S): Krepski, Larry R.; Dellaria, Joseph F., Jr.; Duffy, Daniel E.; Radmer, Matthew R.; Amos, David T.

PATENT ASSIGNEE(S): 3M Innovative Properties Company, USA

SOURCE: PCT Int. Appl., 200 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

Updated Search

STN

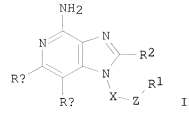
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2005051317	A2	20050609	WO 2004-US39512		20041124
WO 2005051317	A3	20060511			
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
AU 2004293078	A1	20050609	AU 2004-293078		20041124
CA 2547020	A1	20050609	CA 2004-2547020		20041124
EP 1687307	A2	20060809	EP 2004-812098		20041124
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, IS					
BR 2004016936	A	20070116	BR 2004-16936		20041124
CN 1926138	A	20070307	CN 2004-80040954		20041124
JP 2007512370	T	20070517	JP 2006-541697		20041124
SG 148201	A1	20081231	SG 2008-8728		20041124
MX 2006005910	A	20060823	MX 2006-5910		20060524
IN 2006CN01848	A	20070608	IN 2006-CN1848		20060525
KR 2006125818	A	20061206	KR 2006-712734		20060623
ZA 2006005216	A	20070425	ZA 2006-5216		20060623
PRIORITY APPLN. INFO.:			US 2003-524961P	P	20031125
			US 2004-580139P	P	20040616
			WO 2004-US39512	W	20041124

OTHER SOURCE(S): CASREACT 143:26611; MARPAT 143:26611
GI

Updated Search

STN



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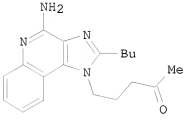

II

AB Title compds. {I; X = alkylene optionally interrupted by one or more -O-; Z = C:O, - C(:O)O-, -C(OR3)2-; R1 = H, (un)substituted alkyl, alkylene/aryl, alkylene/heteroaryl; Q = O, S; R3 = (un)substituted alkyl, alkylene/aryl, alkylene/heteroaryl; R2 = H, (un)substituted alk(en/yn)yl, hetero/aryl, alkylenealkyl, etc.; RA, RB = independently H, halo, alk(en)yl, alkoxy, alkylthio, NH2 and derivs.; or RACCRB = (un)substituted fused aryl ring or fused 5-7-membered saturated ring; and their pharmaceutically acceptable salts}, were prepared as immunomodulators for inducing cytokine biosynthesis in animals and in the treatment of diseases including viral and neoplastic diseases. For example, II was prepared by reacting 4-(2-Butyl-1H-imidazo[4,5-c]quinolin-1-yl)butyraldehyde (preparation given) with MeMgBr, followed by oxidation, reductive amination of the ketone, oxidation with m-CPBA/reaction with NH4OH. I have been found to induce cytokine biosynthesis by inhibiting production of tumor necrosis factor TNF-α when tested on an in vitro human blood cell system (no data).

OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 4 OF 6 HCAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2005:177837 HCAPLUS

DOCUMENT NUMBER: 142:280205

TITLE: Preparation of hydroxylamine substituted imidazo-containing compounds as inducers of cytokine biosynthesis for treatment of viral and neoplastic disease

INVENTOR(S): Kshirsagar, Tushar A.; Amos, David T.; Dellaria, Joseph F., Jr.; Heppner, Philip D.; Langer, Scott E.; Zimmermann, Bernhard M.

PATENT ASSIGNEE(S): 3M Innovative Properties Company, USA

SOURCE: PCT Int. Appl., 254 pp.
CODEN: PIXXD2

Updated Search

STN

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005018556	A2	20050303	WO 2004-US26158	20040812
WO 2005018556	A3	20050929		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004266658	A1	20050303	AU 2004-266658	20040812
CA 2535120	A1	20050303	CA 2004-2535120	20040812
EP 1653955	A2	20060510	EP 2004-780922	20040812
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR				
CN 1835750	A	20060920	CN 2004-80023051	20040812
BR 2004013558	A	20061017	BR 2004-13558	20040812
JP 2007502293	T	20070208	JP 2006-523371	20040812
US 20080114019	A1	20080515	US 2006-595058	20060123
MX 2006001674	A	20060512	MX 2006-1674	20060210

PRIORITY APPLN. INFO.:	US 2003-494605P	P	20030812
	US 2003-494608P	P	20030812
	WO 2004-US26158	W	20040812

OTHER SOURCE(S): CASREACT 142:280205; MARPAT 142:280205
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. [I; X = CHR2, CHR2A; A = (un)substituted alkylene, alkenylene; Y = a bond, C(:O), C(:S), SO2, COO, CONH and derivs., etc.; R1, R' = independently H, (un)substituted alk(en)yl, aryl, etc.; RA, RB = independently H, halo, alk(en)yl, alkoxy, alkylthio, NH2 and derivs.; or RACCRB = (un)substituted fused hetero/aryl, fused 5- to 7-membered saturated ring; R'' = H, non-interfering substituent; and their pharmaceutically acceptable salts], were prepared as immunomodulators for inducing cytokine biosynthesis in animals and in the treatment of diseases including viral and neoplastic diseases. For example, reacting 1-[3-(aminooxy)propyl]-2-propyl-1H-imidazo[4,5-c]quinolin-4-amine (preparation given) with cyclopropanecarbonyl chloride gave title compound II (m.p. = 103-105°). Thus, induced interferon and tumor necrosis factor in human cells (no data).
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

STN

L2 ANSWER 5 OF 6 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2005:177833 HCAPLUS
DOCUMENT NUMBER: 142:280204
TITLE: Preparation of oxime substituted imidazo-containing compounds as inducers of cytokine biosynthesis for treatment of viral and neoplastic disease
INVENTOR(S): Kshirsagar, Tushar; Amos, David T.; Dellaria, Joseph F., Jr.; Heppner, Philip D.; Langer, Scott E.; Zimmermann, Bernhard M.
PATENT ASSIGNEE(S): 3M Innovative Properties Company, USA
SOURCE: PCT Int. Appl., 348 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005018551	A2	20050303	WO 2004-US26065	20040812
WO 2005018551	A3	20060511		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004266641	A1	20050303	AU 2004-266641	20040812
CA 2535117	A1	20050303	CA 2004-2535117	20040812
EP 1653914	A2	20060510	EP 2004-780839	20040812
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BR 2004012902	A	20060926	BR 2004-12902	20040812
JP 2007502288	T	20070208	JP 2006-523340	20040812
CN 101094670	A	20071226	CN 2004-80023366	20040812
US 20070066639	A1	20070322	US 2006-595065	20060126
MX 2006001669	A	20060428	MX 2006-1669	20060210
IN 2006CN00516	A	20070622	IN 2006-CN516	20060210

PRIORITY APPLN. INFO.: US 2003-494605P P 20030812
US 2003-494608P P 20030812
WO 2004-US26065 W 20040812

OTHER SOURCE(S): CASREACT 142:280204; MARPAT 142:280204
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. [I; X = CHR2A; A = alkylene, alkenylene optionally

Updated Search

interrupted by one or more O; R1, R' = independently H, (un)substituted alk(en)yl, hetero/aryl, hetero/arylalkylenyl, heterocyclyl, heterocyclylalkylenyl, etc.; RA, RB = independently H, halo, alk(en)yl, alkoxy, alkylthio, NH2 and derivs.; or RACCRB = (un)substituted fused hetero/aryl, fused 5- to 7-membered saturated ring; R'' = H, non-interfering substituent; and their pharmaceutically acceptable salts], were prepared as immunomodulators for inducing cytokine biosynthesis in animals and in the treatment of diseases including viral and neoplastic diseases. Thus, reacting 4-fluorobenzaldehyde with 1-[3-(aminooxy)propyl]-2-propyl-1H-imidazo[4,5-c]quinolin-4-amine (preparation given) in MeOH gave oxime II. I induced interferon and tumor necrosis factor in human cells (no data).

OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 6 OF 6 HCAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 1949:1122 HCAPLUS

DOCUMENT NUMBER: 43:1122

ORIGINAL REFERENCE NO.: 43:307h-i

TITLE: Effect of normal blood serum and blood serum from neoplastic disease on cell proliferation in bone marrow cultures

AUTHOR(S): Norris, Earl R.; Majnarich, John J.

SOURCE: American Journal of Physiology (1948), 153, 483-7
CODEN: AJPHAP; ISSN: 0002-9513

DOCUMENT TYPE: Journal

LANGUAGE: Unavailable

AB cf. C.A. 42, 7883f. Normal blood serum accelerates the rate of cell proliferation in bone marrow cultures in vitro. Blood serum in cases of pernicious anemia, leukemia and neoplastic disease inhibits cell proliferation in such cultures. The accelerating substance present in normal serum and the inhibiting substance present in blood serum in cases of neoplastic disease counteract each other.

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=> d his

     (FILE 'HOME' ENTERED AT 17:34:06 ON 19 OCT 2009)

     FILE 'HCAPLUS' ENTERED AT 17:34:33 ON 19 OCT 2009
L1          2745 S NEOPLASTIC () DISEASE
L2             6 S L1 () INHIBIT?
L3             0 S L2 AND REVIEW/DT

=> s VEGF () receptor?
         30909 VEGF
           231 VEGFS
         30929 VEGF
                 (VEGF OR VEGFS)
        993539 RECEPTOR?
L4        4213 VEGF (W) RECEPTOR?

=> s l4 () inhibit?
       2189130 INHIBIT?
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STN

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L5          120 L4 (W) INHIBIT?

=> s l5 and neoplast?
         71713 NEOPLAST?
L6           3 L5 AND NEOPLAST?

=> s l6 and review/dt
       2306050 REVIEW/DT
L7           0 L6 AND REVIEW/DT

=> s l5 and review/dt
       2306050 REVIEW/DT
L8          22 L5 AND REVIEW/DT

=> d 18,ibib abs hitstr, 1-22
THE ESTIMATED COST FOR THIS REQUEST IS 124.08 U.S. DOLLARS
DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N:y

L8   ANSWER 1 OF 22  HCAPLUS  COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER:         2009:1181014  HCAPLUS
TITLE:                    Role of everolimus in the treatment of renal cell
                          carcinoma
AUTHOR(S):                George, Saby; Bukowski, Ronald M.
CORPORATE SOURCE:         Division of Hematology and Oncology, University of
                          Texas Health Sciences Center, San Antonio, TX, USA
SOURCE:                   Therapeutics and Clinical Risk Management (2009), 5,
                          699-706
                          CODEN: TCRMA6; ISSN: 1178-203X
                          URL: http://www.dovepress.com/getfile.php?fileID=5207
PUBLISHER:                Dove Medical Press (NZ) Ltd.
DOCUMENT TYPE:            Journal; General Review; (online computer
                          file)
LANGUAGE:                 English
AB   A review.  The therapeutic options in metastatic renal cell carcinoma have
     been recently expanded by the discovery of the VHL gene, the mutation of
     which is associated with development of clear cell carcinoma, and
     overexpression of the angiogenesis pathway, resulting in a very vascular
     tumor.  This breakthrough in science led to the development of a variety
     of small mols. inhibiting the VEGF-dependent angiogenic pathway, such as
     sunitinib and sorafenib.  These agents prolong overall and
     progression-free survival, resp.  The result was the development of robust
     front-line therapies which ultimately fail and are associated with disease
     progression.  In this setting, there existed an unmet need for developing
     second-line therapies for patients with refractory metastatic renal cell
     carcinoma (MRCC).  Everolimus (RAD 001) is an oral inhibitor of the
     mammalian target of rapamycin (mTOR) pathway.  The double-blind,
     randomized, placebo-controlled phase III trial of everolimus (RECORD-1)
     conducted in MRCC patients after progression on sunitinib or sorafenib, or
     both, demonstrated a progression-free survival benefit favoring the study
     drug (4.9 mo vs 1.9 mo, HR 0.33, 95% CI 0.25 to 0.43, P ≤ 0 0.001).
     Everolimus thus established itself as a standard of care in the second-line
     setting for patients with MRCC who have failed treatment with VEGF
     receptor inhibitors.
REFERENCE COUNT:          25    THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS
                                RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT
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L8 ANSWER 2 OF 22 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2009:790381 HCAPLUS
DOCUMENT NUMBER: 151:115426
TITLE: Angiopreventive role of vitamins
AUTHOR(S): Josko, Jadwiga; Ratman, Rajmund; Ratman, Katarzyna
CORPORATE SOURCE: Katedra i Zakl. Med. i Epidemiol. Srodowiskowej Zabrze, Slaski Uniw. Med. Katowice, Zabrze, 41-800, Pol.
SOURCE: Wspolczesna Onkologia (2008), 12(4), 168-172
CODEN: WOSNBU; ISSN: 1428-2526
PUBLISHER: Termedia sp. z o.o. Wydawnictwo Medyczne
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Polish
AB A review. The process of angiogenesis allows neoplasm growth and accelerates tumor metastasis formation. The possibility of using vitamins in angiogenesis control is discussed. In vivo and in vitro studies show that vitamins can inhibit excessive angiogenesis. The mechanisms of angiogenesis inhibition by vitamins involve transcription of genes of angiogenic factors (such as VEGF - vascular endothelial growth factor), decreased expression of VEGF receptors, inhibition of the activation of transcription factors, decrease of angiopoietin 2 levels, increased apoptosis of endothelial cells, glutathione peroxidase inhibition, inhibition of tyrosine kinase activity, etc. The roles of vitamins A, B6, C, D, E, and folic acid are examined in more detail. It is possible that vitamins, whose roles in these mechanisms are underestimated, may significantly support components of antitumor therapy.

L8 ANSWER 3 OF 22 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2009:212953 HCAPLUS
DOCUMENT NUMBER: 151:138934
TITLE: Progress on molecular target therapy of head and neck malignant tumor
AUTHOR(S): Zhou, Xiaojuan; Ma, Hailin
CORPORATE SOURCE: The First Affiliated Hospital, Xian Jiaotong University, Xian, Shaanxi Province, 710061, Peop. Rep. China
SOURCE: Xiandai Zhongliu Yixue (2008), 16(1), 138-140
CODEN: XZYIAU; ISSN: 1672-4992
PUBLISHER: Xiandai Zhongliu Yixue Bianjibu
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Chinese
AB A review. The applications of mol. target drugs in therapy of head and neck malignant tumor were reviewed, including EGFR inhibitions, anti-EGRF monoclonal antibody, VEGF receptor inhibitions , and so on.

L8 ANSWER 4 OF 22 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2008:1408039 HCAPLUS
DOCUMENT NUMBER: 150:468546
TITLE: Vascular endothelial growth factor as new drug target in treatment of multiple myeloma
AUTHOR(S): Luo, Wenjuan; Xu, Wenlin
CORPORATE SOURCE: Renmin Hospital, Jiangsu University, Zhenjiang, 212002, Peop. Rep. China
SOURCE: Zhonghua Xueyexue Zazhi (2007), 28(10), 718-720

CODEN: CHTCD7; ISSN: 0253-2727
PUBLISHER: Zhongguo Yixue Kexueyuan Xueyexue Yanjiuso
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Chinese
AB A review on regulation and pathophysiol. role of vascular endothelial growth factor (VEGF) in multiple myeloma (MM) and MM treatment based on VEGF with thalidomide and VEGF receptor tyrosine kinase inhibitor.

L8 ANSWER 5 OF 22 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2008:166110 HCAPLUS
DOCUMENT NUMBER: 149:214754
TITLE: Angiogenesis inhibitor therapies: focus on hypertension and kidney toxicity
AUTHOR(S): Izzedine, Hassan
CORPORATE SOURCE: Service de Nephrologie, Hopital Pitie-Salpetriere, Paris, F-75013, Fr.
SOURCE: Bulletin du Cancer (2007), 94(11), 981-986
CODEN: BUCABS; ISSN: 0007-4551
PUBLISHER: John Libbey Eurotext
DOCUMENT TYPE: Journal; General Review
LANGUAGE: French
AB A review. Developments in the knowledge of mol. biol. of cancer over the past 20 years have been identified. Angiogenesis is playing a key role in the physiopathol. of cancer evolution. Several strategies have been developed to target angiogenesis for the treatment of metastatic RCC. These include inhibition of VEGF receptors (inhibition of the tyrosine kinase activity) or binding to the VEGF protein. Several addnl. kinases inhibitions including PDGF receptors are also targeted. Anti-angiogenic drugs recently marketed or still under clin. development, may interact with the kidneys. Clin. and pathol., and mechanisms of their renal toxicity are presented in this article.
OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 6 OF 22 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2007:1282475 HCAPLUS
DOCUMENT NUMBER: 148:165032
TITLE: Angiogenesis and renal cell carcinoma
AUTHOR(S): Billemont, Bertrand; Meric, Jean-Baptiste; Izzedine, Hassan; Taillade, Laurent; Sultan-Amar, Valentine; Rixe, Olivier
CORPORATE SOURCE: Service d'oncologie medicale, Hopital Pitie-Salpetriere, Paris, 75013, Fr.
SOURCE: Bulletin du Cancer (2007), 94(Spec.), S232-S240
CODEN: BUCABS; ISSN: 0007-4551
PUBLISHER: John Libbey Eurotext
DOCUMENT TYPE: Journal; General Review
LANGUAGE: French
AB A review. Developments in the knowledge of mol. biol. of renal cell carcinoma (RCC) over the past 20 years have been identified. Angiogenesis is playing a key role in the physiopathol. of RCC. Von Hippel-Lindau (VHL) alterations, HIFα accumulation and vascular endothelial growth factor (VEGF) overexpression are important mediators of this process. Several stategies have been developed to target angiogenesis for the

treatment of metastatic RCC. These include inhibition of VEGF receptors (inhibition of the tyrosine kinase activity) or binding to the VEGF protein. Several addnl. kinases inhibitions including PDGF receptors are also targeted. Sunitinib (SU11248) is an orally biovailable small mol. that has demonstrated superiority over interferon-α for the treatment of metastatic RCC. In a recent randomized phase III study conducted in 750 patients, the response rate to sunitinib was 31 % and to interferon 6 %. The median of progression free survival (PFS) was 11 mo for sunitinib and 5 mo for interferon (p < 0.001). Sorafenib (BAY43-9006) was found to inhibit Raf1, but also VEGFR2 and 3, Flt3, PDGFR-a and b and c-kit, has been tested in a phase III study against placebo after one prior systemic therapy. The median of the time to progression (TTP) for sorafenib was 24 wk vs. 12 wk for patients in the placebo arm (p = 0,01). Other mols. tested in metastatic RCC will be presented including axitinib, pazopanib and bevacizumab.

OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD (4 CITINGS)

REFERENCE COUNT: 76 THERE ARE 76 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 7 OF 22 HCAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2007:798379 HCAPLUS

DOCUMENT NUMBER: 147:108604

TITLE: Inhibition of VEGF signaling pathways in multiple myeloma and other malignancies

AUTHOR(S): Podar, Klaus; Anderson, Kenneth C.

CORPORATE SOURCE: Department of Medical Oncology, Harvard Medical School, Boston, MA, USA

SOURCE: Cell Cycle (2007), 6(5), 538-542
CODEN: CCEYAS; ISSN: 1538-4101

PUBLISHER: Landes Bioscience

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review. Due to its direct effects on endothelial cells, circulatory endothelial progenitor cells, hematopoietic stem cells, immune cells, osteoclasts, osteoblasts and neurons, vascular endothelial growth factor (VEGF) is linked to tumor cell development, progression, metastatic osteolysis and drug resistance, as well as clin. features such as metastatic osteolysis. Importantly, recent advances in the understanding of mechanisms of action of antiangiogenic drugs/VEGF-inhibitors have fundamentally changed treatment regimens in cancer. VEGF plays a key role not only in solid tumors but also in hematol. malignancies, including multiple myeloma (MM). Despite recent advances in our understanding of MM pathogenesis and novel therapies (bortezomib and lenalidomide), it remains incurable. Our own and others' work suggest that VEGF-inhibitors e.g., the small mol. VEGF receptor inhibitor pazopanib, may also improve patient outcome in MM.

OS.CITING REF COUNT: 14 THERE ARE 14 CAPLUS RECORDS THAT CITE THIS RECORD (14 CITINGS)

REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 8 OF 22 HCAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2007:718530 HCAPLUS

DOCUMENT NUMBER: 147:514036

TITLE: CCR drug updates: Sorafenib and sunitinib in renal

cell carcinoma
AUTHOR(S): Stein, Mark N.; Flaherty, Keith T.
CORPORATE SOURCE: Department of Medicine, Robert Wood Johnson Medical School, The Cancer Institute of New Jersey, University of Medicine and Dentistry of New Jersey, New Brunswick, NJ, USA
SOURCE: Clinical Cancer Research (2007), 13(13), 3765-3770 CODEN: CCREF4; ISSN: 1078-0432
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. The role of sorafenib and sunitinib antagonize VEGF receptor tyrosine kinases of these agents as VEGFR inhibitors in renal cell carcinoma (RCC) and their unique spectra of activity are discussed.
OS.CITING REF COUNT: 7 THERE ARE 7 CAPLUS RECORDS THAT CITE THIS RECORD (7 CITINGS)
REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 9 OF 22 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2007:73318 HCAPLUS
DOCUMENT NUMBER: 146:517042
TITLE: Microenvironmental transformations by VEGF- and EGF-receptor inhibition and potential implications for responsiveness to radiotherapy
AUTHOR(S): Bussink, Johan; Kaanders, Johannes H. A. M.; van der Kogel, Albert J.
CORPORATE SOURCE: Department of Radiation Oncology, Radboud University Nijmegen Medical Centre, Neth.
SOURCE: Radiotherapy and Oncology (2007), 82(1), 10-17 CODEN: RAONDT; ISSN: 0167-8140
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. The microregional distribution and dynamics of tumor cell hypoxia and proliferation are important determinants of tumor aggressiveness and resistance to treatment. Modulation of these elements by biol. targeted drugs such as EGFR- and VEGFR-inhibitors may improve the effect of radiotherapy significantly. These combinations are being evaluated in clin. trials and evidence of their effectiveness is accumulating. However, the mechanistic basis of this cooperative effect and the role and behavior of the microregional tumor phenotype under EGF- and VEGF-blockage is poorly understood. Unfolding of these interactions and effects further downstream is necessary to exploit these biol. modifiers most profitably to unravel questions such as: (1) can microregional phenotypes be modulated by EGFR- or VEGFR-blockage and how do downstream effects in the signaling pathways relate to these changes. (2) How do the microregional changes induced by EGFR- and VEGF-blockage affect the responsiveness of tumors to ionizing radiation. Answering these questions will improve our understanding of tumor growth related phenotypic transformations at the microregional level and how these can be influenced by modulation of the EGF- and VEGF-signaling pathways. This knowledge can be used to identify and improve therapeutic combinations with the novel biol. modifiers and test a variety of biol.-based treatment approaches.
OS.CITING REF COUNT: 6 THERE ARE 6 CAPLUS RECORDS THAT CITE THIS RECORD

(6 CITINGS)
REFERENCE COUNT: 88 THERE ARE 88 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 10 OF 22 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2006:1231965 HCAPLUS
DOCUMENT NUMBER: 146:92441
TITLE: The current role of angiogenesis inhibitors in the treatment of renal cell carcinoma
AUTHOR(S): Choueiri, Toni K.; Bukowski, Ronald M.; Rini, Brian I.
CORPORATE SOURCE: Department of Solid Tumor Oncology, Cleveland Clinic Taussig Cancer Center, Cleveland, OH, USA
SOURCE: Seminars in Oncology (2006), 33(5), 596-606
CODEN: SOLGAV; ISSN: 0093-7754
PUBLISHER: Elsevier Inc.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. Over the last few years, renal cell carcinoma (RCC) has become a model disease for targeted therapeutics based on the growing understanding of the underlying mol. pathways in this disease. Clear cell RCC is characterized by the inactivation of the von Hippel-Lindau (VHL) tumor-suppressor gene, which results in the dysregulation of hypoxia response genes, including an overprodn. of vascular endothelial growth factor (VEGF), which promotes tumor angiogenesis, growth, and metastasis. In advanced RCC, substantial clin. activity has been reported with VEGF blockade employing a variety of approaches including antibodies and small-mol. VEGF receptor inhibitors. Many trials are still in progress with the goal of defining the optimal utility of these agents as monotherapy or in combination. This review will describe the current clin. data with VEGF-targeted approaches in RCC and plans for future development.
OS.CITING REF COUNT: 9 THERE ARE 9 CAPLUS RECORDS THAT CITE THIS RECORD (9 CITINGS)
REFERENCE COUNT: 83 THERE ARE 83 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 11 OF 22 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2006:548173 HCAPLUS
DOCUMENT NUMBER: 145:96528
TITLE: Advances in vascular endothelial growth factor and anti-angiogenesis
AUTHOR(S): Chen, Xi; Liu, Lianxin
CORPORATE SOURCE: First Clinical Hospital, Harbin Medical University, Harbin, Heilongjiang Province, 150001, Peop. Rep. China
SOURCE: Shijie Huaren Xiaohua Zazhi (2005), 13(16), 1996-2000
CODEN: SHXZF2; ISSN: 1009-3079
PUBLISHER: Shijie Weichangbingxue Zazhishe
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Chinese
AB A review summarized the structure, function, regulation and inhibitors of VEGF (vascular endothelial growth factor) and its receptor as well as their roles in angiogenesis.

L8 ANSWER 12 OF 22 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2006:205613 HCAPLUS

STN

DOCUMENT NUMBER: 145:179897
TITLE: Medical treatment of Gastrointestinal Stromal Tumors: state of the art and future perspectives
AUTHOR(S): Apice, Gaetano; Milano, Amalia; Bruni, Giovanni Salvatore; Iaffaioli, Rosario Vincenzo; Caponigro, Francesco
CORPORATE SOURCE: National Tumor Institute of Naples "Fondazione G. Pascale", Naples, 80131, Italy
SOURCE: Reviews on Recent Clinical Trials (2006), 1(1), 35-42 CODEN: RRCTB2; ISSN: 1574-8871
PUBLISHER: Bentham Science Publishers Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. Gastrointestinal Stromal Tumor (GIST) is the most common mesenchymal neoplasm of the gastrointestinal tract, and it is characterized by the occurrence, in > 90 % of cases, of a gain of function mutation in the c-kit proto-oncogene. STI-571 (imatinib mesylate), a selective KIT tyrosine kinase inhibitor, has changed the natural history of this disease, since it has shown high effectiveness in metastatic GIST, and it is currently under investigation also in the adjuvant and neoadjuvant setting. Mechanisms of resistance to imatinib mesylate include both de novo, and, more frequently, acquired resistance, which may occur after several months of drug administration and possibly depends, in most cases, upon an acquired second mutation. In order to overcome imatinib mesylate resistance, the addition of other drugs may be considered in patients who have less than an optimal response to imatinib mesylate monotherapy. Investigational agents that are being studied in this setting include the mammalian target of rapamycin (mTOR) inhibitor RAD 001 and the protein kinase C inhibitor PKC412. In addition, other KIT tyrosine kinase inhibitors with anti-VEGF receptor inhibitory activity, such as SU11248, PTK787/ZK787 and AMG 706, are currently being explored as second line monotherapy for imatinib mesylate-resistant GIST. Finally, another new drug, ecteinascidin (ET-743), that blocks cell cycle progression in G2/M phase through a p53-independent apoptotic mechanism, has shown important preclin. and clin. activity against a number of human solid tumors, including GIST.
OS.CITING REF COUNT: 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
REFERENCE COUNT: 64 THERE ARE 64 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 13 OF 22 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2006:50281 HCAPLUS
DOCUMENT NUMBER: 144:362423
TITLE: Molecular mechanisms and targeting of colorectal cancer
AUTHOR(S): Vanhoefer, Udo
CORPORATE SOURCE: Department of Medicine, Medical Oncology and Hematology, Gastroenterology, and Infectious Disease, Marienkrankenhaus, Hamburg, Germany
SOURCE: Seminars in Oncology (2005), 32(6, Suppl. 8), S7-S10 CODEN: SOLGAV; ISSN: 0093-7754
PUBLISHER: Elsevier Inc.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. Targeted therapies that are approved for metastatic colorectal

cancer are divided into two groups: those affecting vascular endothelial growth factor (VEGF) known to interrupt tumor growth and metastasis (also called neo-angiogenesis), and agents that affect the tumor directly by interrupting the epidermal growth factor (EGF) and its receptor. Anti-angiogenic VEGF therapies are divided into two categories: one affecting the VEGF ligand, such as bevacizumab, and those that inhibit the VEGF receptor, such as PTK/ZK. Epidermal growth factor receptor (EGFR) therapies are divided into monoclonal antibodies that affect EGFR, such as cetuximab, and EGFR tyrosine kinase inhibitors, such as gefitinib. Both VEGF and EGFR areas of treatment have shown promising efficacy in first-line, combination therapy settings. Future targeted therapeutic strategies include gene profiling, combinations of capecitabine and oxaliplatin, with bevacizumab and/or cetuximab therapies.

REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 14 OF 22 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2006:40297 HCAPLUS
DOCUMENT NUMBER: 144:444742
TITLE: Cytokine targets in the treatment of myelodysplastic syndromes
AUTHOR(S): Verma, Amit; List, Alan F.
CORPORATE SOURCE: Department of Medicine (Oncology), Albert Einstein Cancer Center, Bronx, NY, 10461, USA
SOURCE: Current Hematology Reports (2005), 4(6), 429-435
CODEN: CHRUEI; ISSN: 1540-3408
PUBLISHER: Current Science Inc.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. Myelodysplastic syndromes (MDS) are characterized by refractory cytopenias due to ineffective hematopoiesis in the marrow. Cytokines play an important role in the regulation of hematopoiesis; dysregulation of their levels can lead to hematopoietic failure. Considerable evidence implicates tumor necrosis factor α, transforming growth factor β, interferons, interleukin 1β, vascular endothelial growth factor (VEGF), and other inhibitory cytokines in the pathogenesis of MDS. These cytokines are produced by the interactions between the MDS clone and the bone marrow microenvironment. Therapeutic strategies therefore may augment the action of stimulatory growth factors or disrupt the effects of myelosuppressive cytokines. Erythropoietin alone and in combination with low-dose granulocyte colony-stimulating factor can lead to erythroid responses in selected patients. Agents targeting inhibitory cytokines include thalidomide, lenalidomide, etanercept, infliximab, VEGF receptor inhibitor PTK-787, antithymocyte globulin, and SCIO-469, a p38 mitogen-activated protein kinase inhibitor. Given the biol. heterogeneity of MDS, no single treatment is effective for all patients with the disease. With more detailed knowledge of cytokine signaling cascades, coupled with technol. improvements in genomics and proteomics, the future treatment of this challenging disease may lie in combination therapies customized for relevant biol. effectors.

OS.CITING REF COUNT: 8 THERE ARE 8 CAPLUS RECORDS THAT CITE THIS RECORD (8 CITINGS)
REFERENCE COUNT: 57 THERE ARE 57 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 15 OF 22 HCAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2005:993266 HCAPLUS
DOCUMENT NUMBER: 144:16256
TITLE: Therapy targeted at vascular endothelial growth factor in metastatic renal cell carcinoma: biology, clinical results and future development
AUTHOR(S): Rini, Brian I.; Sosman, Jeffrey A.; Motzer, Robert J.
CORPORATE SOURCE: Taussig Cancer Center, Cleveland Clinic Foundation, USA
SOURCE: BJU International (2005), 96(3), 286-290
CODEN: BJINFO; ISSN: 1464-4096
PUBLISHER: Blackwell Publishing Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. A growing understanding of the underlying biol. of renal cell carcinoma (RCC) has identified vascular endothelial growth factors a logical therapeutic target. Therapy directed against the biol. activity of VEGF has undergone initial clin. testing in metastatic RCC, with evidence of a substantial antitumor effect. Biol. of VEGF expression in RCC, clin. results of VEGF-targeted therapy in RCC, anti-VEGF antibody (bevacizumab), small-mol. VEGF receptor inhibitors, and ongoing clin. trials of VEGF-targeted therapy in RCC are discussed.
OS.CITING REF COUNT: 20 THERE ARE 20 CAPLUS RECORDS THAT CITE THIS RECORD (20 CITINGS)
REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 16 OF 22 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2004:649278 HCAPLUS
DOCUMENT NUMBER: 142:277392
TITLE: VEGF-targeted therapy
AUTHOR(S): Takahashi, Yutaka; Mai, Masayoshi
CORPORATE SOURCE: Cancer Research Institute, Kanazawa University, Japan
SOURCE: Gendai Iryo (2004), 36(7), 1481-1485
CODEN: GEIRDK; ISSN: 0533-7259
PUBLISHER: Gendai Iryosha
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Japanese
AB A review. The topics discussed are (1) angiogenic mitogen vascular endothelial growth factor (VEGF) and VEGF targeted therapy; (2) efficacy of VEGF antibody bevacizumab against metastatic colon cancer; (3) effect of VEGF antibody on other tumors; and (4) VEGF family and VEGF receptor inhibitors.

L8 ANSWER 17 OF 22 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2004:504576 HCAPLUS
DOCUMENT NUMBER: 142:131536
TITLE: Angiogenesis in multiple myeloma
AUTHOR(S): Uneda, Shima; Hata, Hiroyuki
CORPORATE SOURCE: Dep. of Immunology, Roswell Park Cancer Institute, Buffalo, NY, USA
SOURCE: Ketsueki, Shuyoka (2004), 48(3), 268-273
CODEN: KETSBI; ISSN: 0915-8529
PUBLISHER: Kagaku Hyoronsha
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Japanese

STN

AB A review. The topics discussed are (1) bone marrow angiogenesis in multiple myeloma; (2) clin. significance of microvessel d.; (3) vascular endothelial growth factor (VEGF), angiopoietin, hepatocyte growth factor (HGF), nitric oxide (NO) in bone marrow angiogenesis in multiple myeloma; and (4) thalidomide and VEGF receptor inhibitor in the inhibition of angiogenesis for the treatment of multiple myeloma.

L8 ANSWER 18 OF 22 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2004:78652 HCAPLUS
DOCUMENT NUMBER: 141:291249
TITLE: Novel radiosensitizers for locally advanced epithelial tumors: inhibition of the PI3K/Akt survival pathway in tumor cells and in tumor-associated endothelial cells as a novel treatment strategy?
AUTHOR(S): Riesterer, Oliver; Tenzer, Angela; Zingg, Daniel; Hofstetter, Barbara; Vuong, Van; Pruschy, Martin; Bodis, Stephan
CORPORATE SOURCE: Department of Radiation Oncology, University Hospital Zurich, Zurich, CH-8091, Switz.
SOURCE: International Journal of Radiation Oncology, Biology, Physics (2004), 58(2), 361-368
CODEN: IOBPD3; ISSN: 0360-3016
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. In locally advanced epithelial malignancies, local control can be achieved with high doses of radiotherapy (RT). Concurrent chemoradiotherapy can improve tumor control in selected solid epithelial adult tumors; however, treatment-related toxicity is of major concern and the therapeutic window often small. Therefore, novel pharmacol. radiosensitizers with a tumor-specific mol. target and a broad therapeutic window are attractive. Because of clonal heterogeneity and the high mutation rate of these tumors, combined treatment with single mol. target radiosensitizers and RT are unlikely to improve sustained local tumor control substantially. Therefore, radiosensitizers modulating entire tumor cell survival pathways in epithelial tumors are of potential clin. use. We discuss the preclin. efficacy and the mechanism of three different, potential radiosensitizers targeting the PTEN/PI3K/Akt survival pathway. These compds. were initially thought to act as single-target agents against growth factor receptors (PKI 166 and PTK 787) or protein kinase C isoforms (PKC 412). We describe an addnl. target for these compds. PKI 166 (an epidermal growth factor [EGF] receptor inhibitor) and PKC 412, target the PTEN/PI3K/Akt pathway mainly in tumor cells, and PTK 787 (a vascular endothelial growth factor [VEGF] receptor inhibitor) in endothelial cells. Even for these broader range mol. radiosensitizers, the benefit could be restricted to human epithelial tumor cell clones with a distinct mol. profile. Therefore, these potential radiosensitizers have to be carefully tested in specific model systems before introduction in early clin. trials.
OS.CITING REF COUNT: 9 THERE ARE 9 CAPLUS RECORDS THAT CITE THIS RECORD (9 CITINGS)
REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 19 OF 22 HCAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2003:951423 HCAPLUS
DOCUMENT NUMBER: 140:52431
TITLE: VEGF-receptor inhibitors for anti-angiogenesis
AUTHOR(S): Shibuya, Masabumi
CORPORATE SOURCE: Inst. Med. Sci., Univ. Tokyo, Tokyo, 108-8639, Japan
SOURCE: Nippon Yakurigaku Zasshi (2003), 122(6), 498-503
CODEN: NYKZAU; ISSN: 0015-5691
PUBLISHER: Nippon Yakuri Gakkai
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Japanese
AB A review. Angiogenesis is deeply involved in the progression of major diseases such as cancer, diabetes, and rheumatoid arthritis. Mol. mechanism on angiogenesis was extensively studied, and several signaling systems including VEGF (VEGF-A), angiopoietin, PDGF, and ephrin were shown to be crucial for physiol. angiogenesis. Interestingly, among these factors, VEGF appears to play key roles in most of the pathol. angiogenesis, and other factors are considered to have addnl. effects on its development depending on the situation. VEGF binds and activates two tyrosine kinase receptors, VEGFR-1 (Flt-1) and VEGFR-2 (KDR/Flk-1), and stimulates endothelial cell growth, survival, and vascular permeability. VEGF induces not only tumor angiogenesis but also blood-vessel-dependent metastasis. Based on the importance of VEGF in diseases, many companies and institutes are now trying to generate appropriate small mols. as well as proteins that strongly antagonize the VEGF-VEGFR system. Several mols. quite effective for suppression of tumorigenesis and pathol. angiogenesis in animal models are under clin. trials.
OS.CITING REF COUNT: 10 THERE ARE 10 CAPLUS RECORDS THAT CITE THIS RECORD (10 CITINGS)

L8 ANSWER 20 OF 22 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2003:791933 HCAPLUS
DOCUMENT NUMBER: 140:233226
TITLE: Metastasis and angiogenesis: recent researches and clinical implication of VEGF and VEGFR
AUTHOR(S): Takahashi, Yutaka; Kitadai, Yasuhiko; Mai, Masayoshi
CORPORATE SOURCE: Cancer Research Institute, Kanazawa University, Japan
SOURCE: Igaku no Ayumi (2003), 206(4), 261-264
CODEN: IGAYAY; ISSN: 0039-2359
PUBLISHER: Ishiyaku Shuppan
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Japanese
AB A review. The topics discussed are (1) vascular endothelial growth factor (VEGF) family members and VEGF receptors; (2) VEGF in promoting lymphangiogenesis; (3) VEGF and its receptor KDR targeted treatment for human colon cancer; (4) anti-VEGF antibodies for cancer treatments; and (5) VEGF receptor inhibitors for cancer treatments.

L8 ANSWER 21 OF 22 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2003:553652 HCAPLUS
DOCUMENT NUMBER: 139:332110
TITLE: Vascular endothelial growth factor receptor tyrosine kinase inhibitors: PTK787/ZK 222584
AUTHOR(S): Thomas, Anne L.; Morgan, Bruno; Drevs, Joachim; Unger, Clemens; Wiedenmann, Bertram; Vanhoefer, Udo; Laurent,

Dirk; Dugan, Margaret; Steward, William P.
CORPORATE SOURCE: Leicester Royal Infirmary, Leicester, UK
SOURCE: Seminars in Oncology (2003), 30(3, Suppl. 6), 32-38
CODEN: SOLGAV; ISSN: 0093-7754
PUBLISHER: W. B. Saunders Co.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. PTK787/ZK 222584 (PTK/ZK) is an oral potent and selective inhibitor of the vascular endothelial growth factor (VEGF)-mediated Flt-I and KDR receptor tyrosine kinases. PTK/ZK has been shown to reduce growth and microvasculature in s.c. implanted human tumor xenografts in nude mice. A clin. difficulty in evaluating angiogenesis inhibitors has been the usefulness of conventional study endpoints. Therefore, dynamic contrast-enhanced magnetic resonance imaging (DCE-MRI) has been studied as a pharmacodynamic marker of efficacy of PTK/ZK. Phase I studies are under way evaluating the optimum dose and schedule of oral PTK/ZK administered continuously to patients with advanced cancers of types known to overexpress VEGF. To date, particularly in patients with liver metastases from colorectal cancer treated with PTK/ZK, DCE-MRI has been a useful predictor of the biol. response of VEGF-receptor inhibition. Toxicities have been manageable and have included lightheadedness, ataxia, nausea, vomiting, and hypertension. Stabilization of disease for ≥6 mo has been seen in heavily pretreated patients receiving PTK/ZK at higher doses. Preliminary data suggest that PTK/ZK can be administered safely on a continuous daily dosing schedule, efficacy data look promising, and DCE-MRI correlates with biol. response. DCE-MRI will be used to guide dose optimization of PTK/ZK and perhaps of other angiogenesis inhibitors in future studies.
OS.CITING REF COUNT: 52 THERE ARE 52 CAPLUS RECORDS THAT CITE THIS RECORD (52 CITINGS)
REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 22 OF 22 HCAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2000:257676 HCAPLUS
DOCUMENT NUMBER: 133:26379
TITLE: Less is more, regularly: metronomic dosing of cytotoxic drugs can target tumor angiogenesis in mice
AUTHOR(S): Hanahan, Douglas; Bergers, Gabriele; Bergsland, Emily
CORPORATE SOURCE: Department of Biochemistry and Biophysics, Hormone Research Institute, University of California San Francisco, San Francisco, CA, USA
SOURCE: Journal of Clinical Investigation (2000), 105(8), 1045-1047
CODEN: JCINAO; ISSN: 0021-9738
PUBLISHER: American Society for Clinical Investigation
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with 23 refs. Chemotherapeutic drugs, long the mainstay of cancer treatment, cause DNA damage and disrupt DNA replication in proliferating cells. Drug regimens have been designed to kill as many tumor cells as possible by treating with "maximum tolerated doses" (MTD5) of these cytotoxic agents. Side effects such as neurotoxicity and damage to proliferating cells in healthy tissues pose serious constraints on the use of chemotherapy. The harsh side effects and the ultimate failures of most chemotherapies have fueled broad investigation of alternatives, including

drugs that target not the transformed tumor cells themselves, but rather a genetically stable constituent cell type of tumors, the endothelial cells that form blood vessels. Angiogenesis, the process by which new blood vessels are formed, is a hallmark capability of cancer; a compelling body of evidence argues that tumor growth depends on the vasculature, and, in particular, on continuing angiogenesis. In particular, metronomic dosing with cytotoxic drugs, while demonstrably antiangiogenic, seem unlikely to prove efficacious in general as single agents. Nevertheless, we believe that metronomic delivery of lowered doses of cytotoxic drugs could be devised to minimize often devastating side effects of chemotherapy, while targeting endothelial and tumor cells. True efficacy may come only with combinatorial therapies, wherein novel cytotoxic dosing schedules are used in conjunction with other drugs or radiation. Possible combinations include other approved drugs, such as cox-2 inhibitors, thalidomide, or IFN-α/β, as well as exptl. drugs such as VEGF/ VEGF-receptor inhibitors, other angiogenesis inhibitors (e.g., TNP-470), proapoptotic drugs, or biotherapeutic agents such as oncolytic viruses. The possibilities raised by these studies are provocative and deserve further preclin. and clin. investigation.

OS.CITING REF COUNT: 205 THERE ARE 205 CAPLUS RECORDS THAT CITE THIS RECORD (205 CITINGS)

REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT